LETTER

Where Have the Fluxes Gone?

In a recently published *Journal of Biological Chemistry* article, Vendelin *et al.* (1) show that total creatine kinase (CK) unidirectional flux decreased by a factor of 2 at the increased energy demand of Langendorff-perfused heart. These results and their interpretation are not consistent with a large body of existing data (2–5). By introducing ^{18}O isotopes into P_i and observing the shift in ^{31}P NMR spectra, *in vivo* energy fluxes via phosphoryl group transfer catalyzed by CK, adenylate kinase (AK), and glycolytic (GL) networks (3–5) have been measured (4, 5). The fluxes through all of these networks increased linearly with workload on the heart, with the CK flux increasing from about 40 nmol/min/mg of protein in resting state to about 300 nmol/min/mg of protein at a 30,000 mm Hg × beats/min workload (4, 5).

Vendelin *et al.* (1) now are the first observing a dramatic decrease of total unidirectional CK flux by increasing the workload, and no mention regarding AK or GL fluxes was made. Where then have all these fluxes gone? The reason may be found in a combination of an elevated Ca^{2+} concentration of 4.0 mM together with isoprenaline: total content of ATP decreased from 7.78 to 4.7 mM. Respiration rate achieved by these drastic means was 75 μmol of O_2/min/g dry weight, less than one-half of maximal respiration rates 168 μmol of O_2/min/g dry weight obtained in experiments with a working heart model without any changes in ATP content (6). Thus, CK is likely to be inactivated and even released from the damaged cells in the Vendelin *et al.* (1) study.

Mayis Aliev[‡], Uwe Schlattner[§], Petras Dzeja[¶], Theo Wallimann[‖], and Valdur Saks[§1]

[‡]Cardiology Research Center, Moscow, Russia, [§]J. Fourier University, Grenoble, France, [¶]Mayo Clinic College of Medicine, Rochester, Minnesota, and [‖]Institute of Cell Biology, Zurich, Switzerland

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[1]E-mail: Valdur.Saks@ujf-grenoble.fr